

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of :

Masaya TANAKA

Art Unit: 3771

Application No. 10/519,941

Examiner: C. T. OSTRUP

Filed: December 29, 2004

For: CARBON DIOXIDE EXTERNAL ADMINISTRATION DEVICE

**DECLARATION OF MASAYA TANAKA UNDER 37 C.F.R. 1.132**

Honorable Commissioner for Patents

Sir

I, Masaya TANAKA, a citizen of Japan, declare as follows:

I graduated from Graduate School of Engineering Osaka University, majored in chemistry and obtained BSc and MSc degrees from the above university March, 1978 and March, 1980 respectively.

From 1980, I was employed in Kanebo Co. Ltd., and engaged in research and development on external drugs.

After leaving the said company in 1997, I made my own research in transdermal drug delivery technique in Kobe Pharmaceuticals University for three years.

I am an inventor of this US Application No. 10/519,941 filed on December 29, 2004, and familiar with the subject matter thereof.

I, Masaya TANAKA, am also one of inventors listed in the cited patent US6,689,339, acknowledges this fact , and explains the significant distinctions between the present invention and the cited patent US6,689,339.

**Comparative Experiment**

**1. Purpose of the Experiment**

This experiment was conducted to compare the vasodilation ability of the present invention and the cited patent US6,689,339.

Vasodilation (that is, Blood Perfusion Increase) is the key feature of CO<sub>2</sub> therapy.

The following experiment was entirely directed and supervised by the inventor of the present invention, Masaya Tanaka.

**2. Present Invention**

Example 2 as described at pages 25-26 of the above-identified

application was carried out. However, in order to determine an ability for Blood Perfusion Increase by Laser Doppler Blood Perfusion Monitor, modification of Example 2 was slightly done. Modification was as follows.

- (i) Sealing enclosure member / Plastic glove
- (ii) Carbon dioxide supply means / CO<sub>2</sub> cylinder
- (iii) Upper arm / hand.

[Example 2]

(Sealing enclosure member)

Plastic glove was used as a sealing enclosure member.

(Carbon dioxide supply means)

CO<sub>2</sub> cylinder was used as a carbon dioxide supply means.

(Carbon dioxide absorption aid)

A viscous material was prepared by using 1.8 g of sodium alginate, 1 g of sodium carboxymethylcellulose, 0.2 g of methylparaben, and 97 ml of purified water, and this viscous material was used as a carbon dioxide absorption aid.

(Procedure)

1 g of the aforementioned absorption aid was applied to cover the left hand of the subject A (46-year-old female).

The left hand was covered with a plastic glove.

A plastic tube connected to the CO<sub>2</sub> cylinder was inserted into the sealing enclosure member and the glove was closed at the wrist with an elastic band.

CO<sub>2</sub> was injected and the blood perfusion was monitored and recorded automatically.

This Procedure was carried out about Subject B (37-year-old female), too.

3. Cited Patent US6,689,339

Example 299 of the cited patent US6,689,339 has a process in which CO<sub>2</sub> is blown into and a composition of Example 299 is viscous. From this point of view, Example 299 is similar to the present invention. Therefore, Example 299 was selected in the cited patent US6,689,339.

Example 299 of the cited patent US6,689,339 was carried out on a one-tenth scale.

[Example 299]

1.2 g of Sodium bicarbonate, 2 g of Carboxymethyl starch

sodium, and 2 g of Sodium alginate was dissolved in 100 ml of Water to provide a first mixture.

Enough amount of CO<sub>2</sub> was blown into the first mixture for 30 minutes, and 2 g of Carboxymethylcellulose was added to and mixed with the first mixture to provide a final mixture. Carboxymethylcellulose was dissolved completely in 30 minutes. CO<sub>2</sub> was expected to be dissolved at saturated concentration (0.1%).

(Procedure)

1g of the final mixture was applied to cover the right hand of the subject A (46-year-old female).

The left hand was covered with a plastic glove same as that of Example 2 of the present invention.

The glove was closed at the wrist with an elastic band same as that of Example 2 of the present invention.

This Procedure was carried out about Subject B (37-year-old female), too.

#### 4. Measurement and Result

The effect of CO<sub>2</sub> is an increase in blood flow. The increase in blood flow appears as an increase in skin temperature. When the skin temperature increases, the activity of the skin cell is activated, and the skin moisture content and the sebum output increase naturally (See [0094]-[0097] in page 6 of US2005/0254993 A1). Therefore, the skin temperature was measured.

[Measurement]

(Example 2 of the present invention)

After 10 minutes CO<sub>2</sub> injection, skin temperature of the left hand was measured. The measurement was carried out by a "Laser Blood Flow Meter OMEGA ZONE OZ-1" made by OMEGAWAVE Inc. The skin temperature was determined as Average value. The average value was determined by performing the measurement 33 times in succession in condition that the measurement once in one second was performed and averaging the 33 measurement values.

(Example 299 of the cited patent US6,689,339)

After 10 minutes application, skin temperature of the left hand was measured in the same manner as Example 2 of the present invention.

[Result]

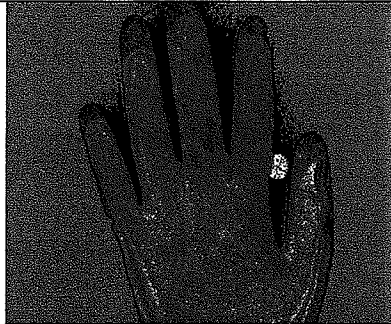

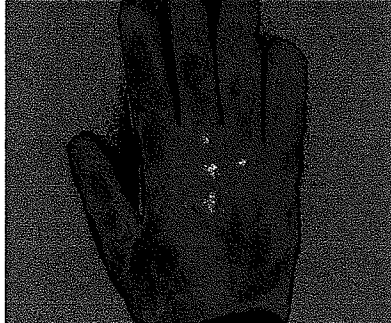
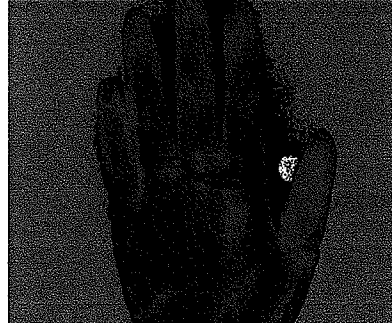
The skin temperatures were shown in Table 1.

(Table 1)

	Skin Temperature(°C)	
	Subject A	Subject B
Example 2 of the present invention	34.87	28.76
Example 299 of the cited patent US6,689,339	20.57	13.06

Blood Flow Images almost corresponding to the Skin Temperature shown in Table 1 were shown in Table 2.

(Table 2)

	Skin Temperature	
	Subject A	Subject B
Example 2 of the present invention		
Example 299 of the cited patent US6,689,339		

## 5. Conclusion

The result shown in Tables 1, 2 clearly indicates that the vasodilation ability of the present invention is superior to that of the cited patent US6,689,339.

Incidentally, Sodium alginate was used in the above described experiment. However, even if Propylene glycol alginate is used instead of Sodium alginate, the result similar to that of the above described experiment may be obtained. The reason is as follows. That is, Propylene glycol alginate is an ester compound of Sodium alginate. Sodium alginate and Propylene glycol alginate are used as thickener in the field of cosmetics and have no difference in the

nature from the viewpoint of thickener. In the field of food, particularly in the food having high calcium concentration, Sodium alginate tends to become gel, and therefore, Propylene glycol alginate is preferably used. However, the present invention is unrelated to calcium. Therefore, in the present invention, that is, in the field of cosmetics, Sodium alginate and Propylene glycol alginate can be preferably used and which thickener to use merely depends on user's taste.

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so that made are punishable by fine or imprisonment, or both, under 18 U.S. Code 1001 and that such willful false statements may be jeopardize the validity of this application or any patent issuing thereon.



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Masaya TANAKA

Dated this 18<sup>th</sup> day of January, 2010